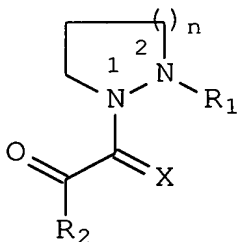


Sub  
A'

- # I

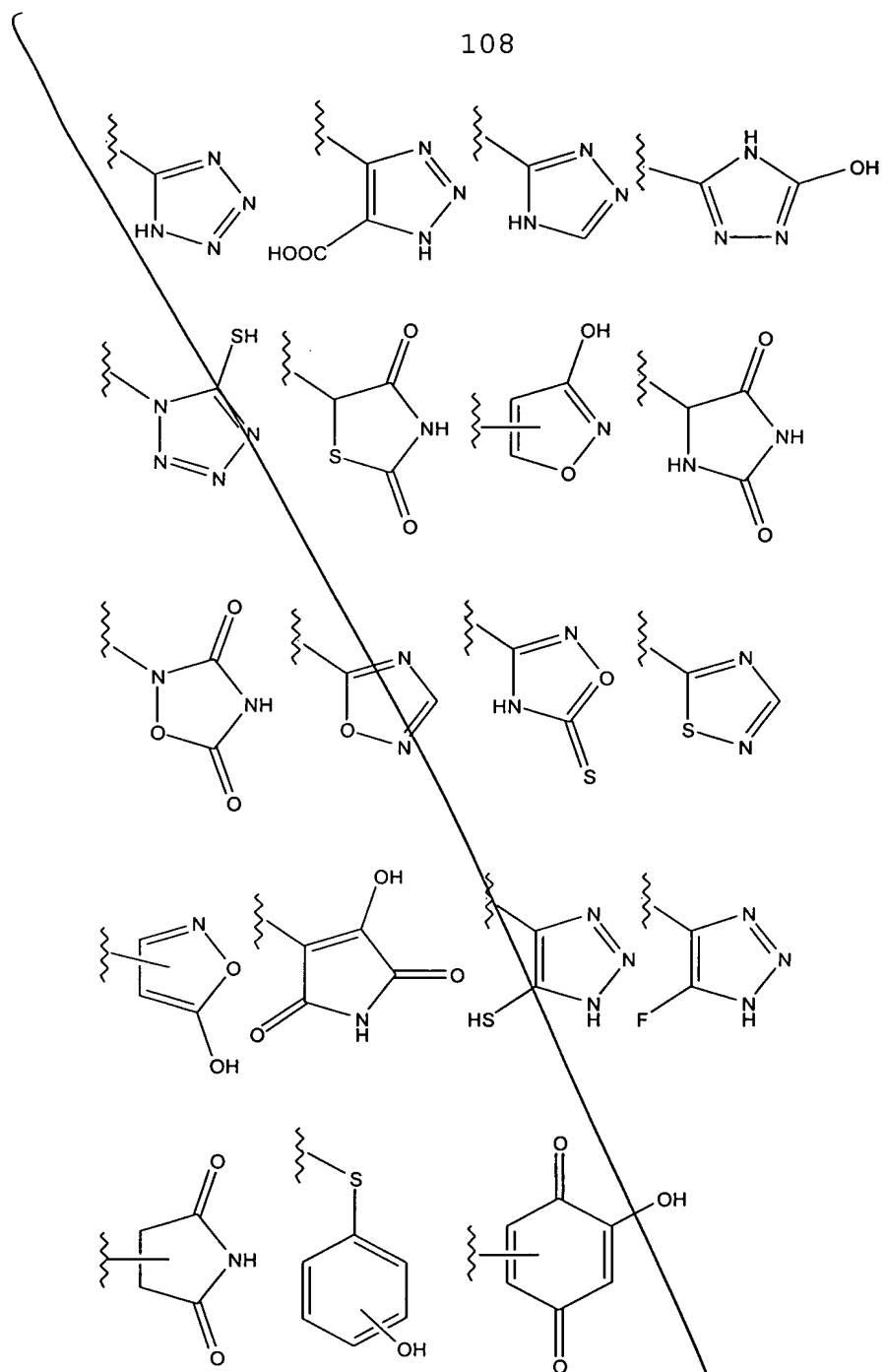


5

n is 1-3;

10

[illegible]



wherein said R<sub>1</sub> group is either unsubstituted or additionally substituted with R<sub>3</sub>;

5 R<sub>2</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkynyl, aryl,

heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituents selected from R<sub>3</sub>;

5 R<sub>3</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkynyl, C<sub>1</sub>-C<sub>9</sub> alkoxy, C<sub>2</sub>-C<sub>9</sub> alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C<sub>1</sub>-C<sub>9</sub> thioalkyl, C<sub>2</sub>-C<sub>9</sub> thioalkenyl, C<sub>1</sub>-C<sub>9</sub> alkylamino, C<sub>2</sub>-C<sub>9</sub> alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

10 wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group; and

20 X is O or S.

2. The compound of claim 1, wherein the compound is non-immunosuppressive.

25 3. The compound of claim 1, wherein said compound is selected from the group consisting of:

3,3-dimethyl-N-[2-(5-phenylpentanoyl)-tetrahydro-1H-1-pyrazolyl]-1,2-pentanedione;

Sub  
C1

# THESE

**THE UNIVERSITY OF CHICAGO**

**Q**uestions

4 - p h e n y l b u t y l      2 - ( 3 , 3 - d i m e t h y l - 2 -  
oxopentanoyl)perhydropyridazinecarboxylate;

5-phenylpentyl 2-(3,3-dimethyl-2-oxopentanoyl)-  
perhydropyridazinecarboxylate;

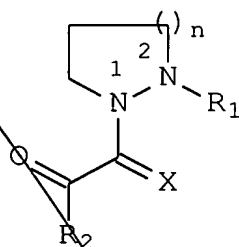
4-(3-pyridyl)butyl 2-(3,3-dimethyl-2-oxopentanoyl)-  
perhydropyridazinecarboxylate;

3,3-dimethyl-1-[2-({5-phenyl}pentanoyl)perhydro-  
pyridazinyl]pentane-1,2-dione; and

pharmaceutically acceptable salts, esters and solvates  
thereof.

10 4. A pharmaceutical composition comprising:

(i) a therapeutically effective amount of a compound of  
formula I:



I

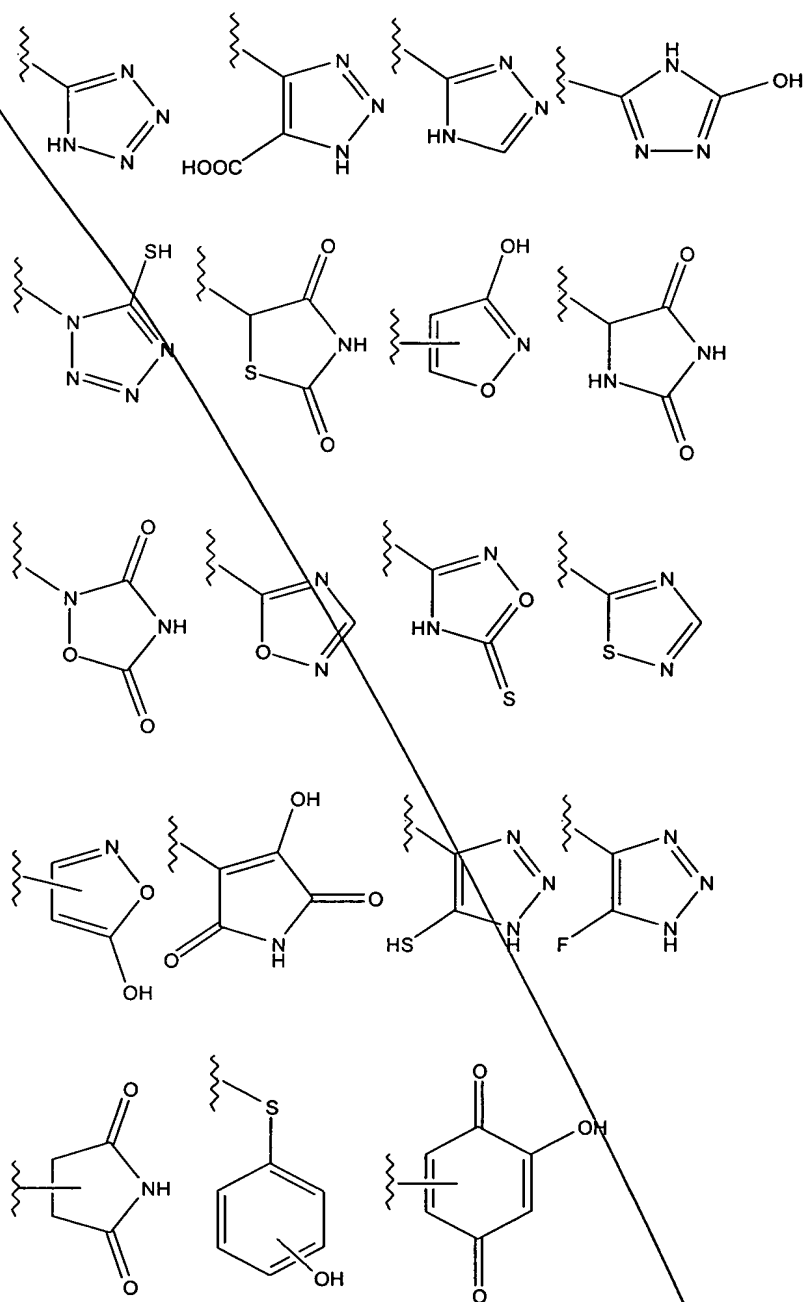
15 or a pharmaceutically acceptable salt, ester or solvate  
thereof, wherein:

n is 1-3;

R<sub>1</sub> is selected from the group consisting of -CR<sub>3</sub>, -COOR<sub>3</sub>,  
-COR<sub>3</sub>, -COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sub>3</sub>, -PO<sub>2</sub>(R<sub>3</sub>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sub>3</sub>)<sub>2</sub>, -OR<sub>3</sub>, -  
SR<sub>3</sub>, -NHCOR<sub>3</sub>, -N(R<sub>3</sub>)<sub>2</sub>, -CON(R<sub>3</sub>)<sub>2</sub>, -CONH(O)R<sub>3</sub>, -CONHNHSO<sub>2</sub>R<sub>3</sub>, -  
COHNSO<sub>2</sub>R<sub>3</sub>, -CONR<sub>3</sub>CN,

Sub  
A2

The diagram illustrates the experimental design. It shows a sequence of events for a single trial: a stimulus (represented by a word or picture), a response (indicated by an arrow), a feedback phase (a green box with a checkmark), and a reward (a coin). This sequence is repeated for multiple trials, as indicated by the 'n' at the end of the sequence.



wherein said R<sub>1</sub> group is either unsubstituted or additionally substituted with R<sub>3</sub>;

5 R<sub>2</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkynyl, aryl,

heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituents selected from R<sub>3</sub>;

R<sub>3</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkynyl, C<sub>1</sub>-C<sub>9</sub> alkoxy, C<sub>2</sub>-C<sub>9</sub> alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C<sub>1</sub>-C<sub>9</sub> thioalkyl, C<sub>2</sub>-C<sub>9</sub> thioalkenyl, C<sub>1</sub>-C<sub>9</sub> alkylamino, C<sub>2</sub>-C<sub>9</sub> alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group; and

X is O or S; and

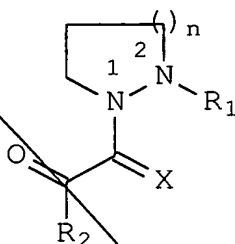
(ii) a pharmaceutically acceptable carrier.

5. The pharmaceutical composition of claim 4, further comprising an additional neurotrophic factor.

6. The pharmaceutical composition of claim 5, wherein the additional neurotrophic factor is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor,

Sub  
C1 insulin growth factor, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factor, neurotrophin-3, neurotrophin-4 and neurotrophin-5.

5 7. A method for effecting a neuronal activity in a mammal, comprising administering to the mammal an effective amount of a compound of formula I:

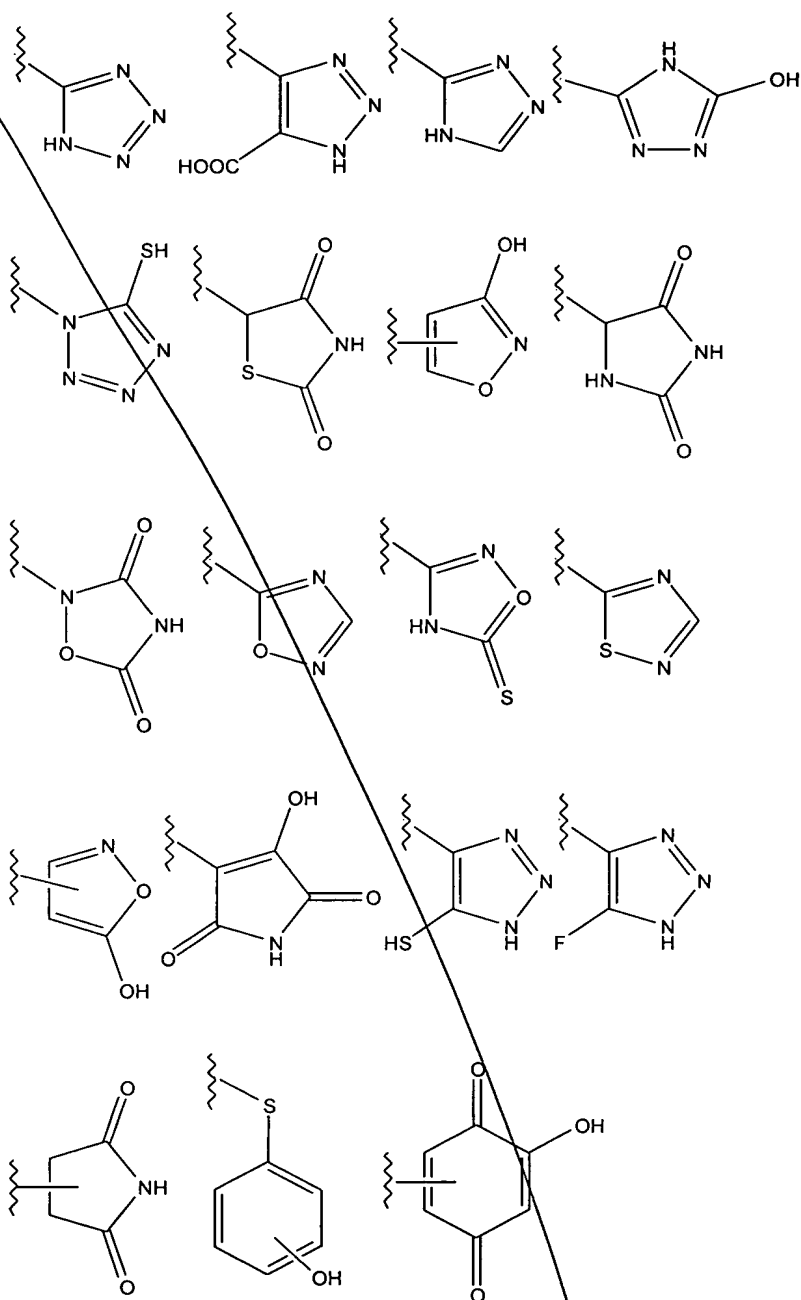


10 or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n is 1-3;

15 R<sub>1</sub> is selected from the group consisting of -CR<sub>3</sub>, -COOR<sub>3</sub>, -COR<sub>3</sub>, -COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sub>3</sub>, -PO<sub>2</sub>(R<sub>3</sub>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sub>3</sub>)<sub>2</sub>, -OR<sub>3</sub>, -SR<sub>3</sub>, -NHCOR<sub>3</sub>, -N(R<sub>3</sub>)<sub>2</sub>, -CON(R<sub>3</sub>)<sub>2</sub>, -CONH(O)R<sub>3</sub>, -CONHNHSO<sub>2</sub>R<sub>3</sub>, -COHNSO<sub>2</sub>R<sub>3</sub>, -CONR<sub>3</sub>CN,





wherein said  $R_1$  group is either unsubstituted or additionally substituted with  $R_3$ ;

$R_2$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  straight or branched chain alkyl,  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_2$ - $C_9$  straight or branched chain alkynyl, aryl,

Sub A3  
heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituents selected from R<sub>3</sub>;

5 R<sub>3</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkynyl, C<sub>1</sub>-C<sub>9</sub> alkoxy, C<sub>2</sub>-C<sub>9</sub> alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C<sub>1</sub>-C<sub>9</sub> thioalkyl, C<sub>2</sub>-C<sub>9</sub> thioalkenyl, C<sub>1</sub>-C<sub>9</sub> alkylamino, C<sub>2</sub>-C<sub>9</sub> alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, 10 sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, 15 alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or 20 heterocycle group; and

X is O or S.

Sub C1  
25 8. The method of claim 7, wherein the neuronal activity is selected from the group consisting of stimulation of damaged neurons, promotion of neuronal regeneration, prevention of neurodegeneration, and treatment of a neurological disorder.

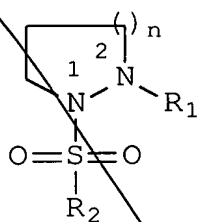
30 9. The method of claim 8, wherein the neurological disorder is selected from the group consisting of peripheral

neuropathy caused by physical injury or disease state, traumatic injury to the brain, physical damage to the spinal cord, stroke associated with brain damage, and a neurological disorder relating to neurodegeneration.

5

10. The method of claim 11, wherein the neurological disorder relating to neurodegeneration is selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis.

11. A compound of formula II:

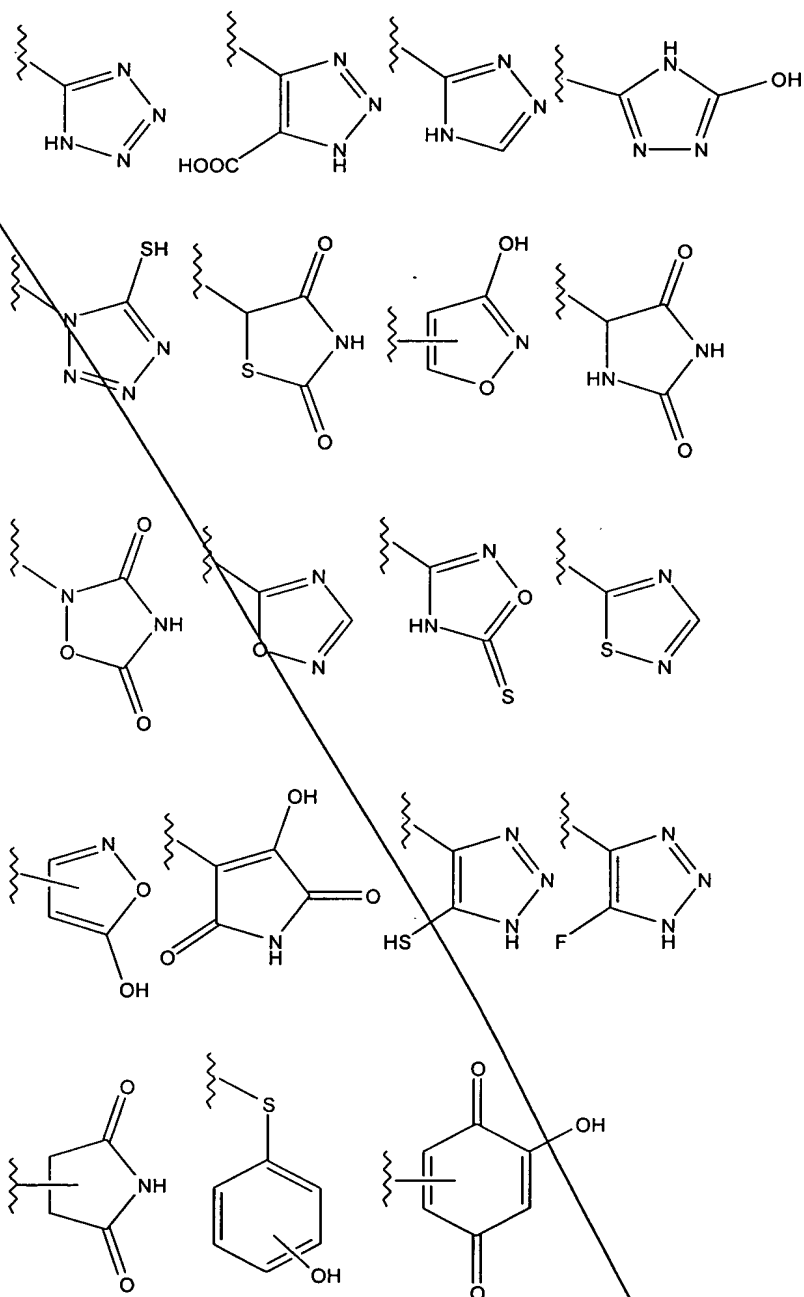


II

or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n is 1-3;

R<sub>1</sub> is selected from the group consisting of -CR<sub>3</sub>, -COOR<sub>3</sub>, -COR<sub>3</sub>, -COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sub>3</sub>, -PO<sub>2</sub>(R<sub>3</sub>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sub>3</sub>)<sub>2</sub>, -OR<sub>3</sub>, -SR<sub>3</sub>, -NHCOR<sub>3</sub>, -N(R<sub>3</sub>)<sub>2</sub>, -CON(R<sub>3</sub>)<sub>2</sub>, -CONH(O)R<sub>3</sub>, -CONHNHSO<sub>2</sub>R<sub>3</sub>, -COHNSO<sub>2</sub>R<sub>3</sub>, -CONR<sub>3</sub>CN,



wherein said  $R_1$  group is either unsubstituted or additionally substituted with  $R_3$ ;

$R_2$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  straight or branched chain alkyl,  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_2$ - $C_9$  straight or branched chain alkynyl, aryl,

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heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituents selected from R<sub>3</sub>; and

5 R<sub>3</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkynyl, C<sub>1</sub>-C<sub>9</sub> alkoxy, C<sub>2</sub>-C<sub>9</sub> alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C<sub>1</sub>-C<sub>9</sub> thioalkyl, C<sub>2</sub>-C<sub>9</sub> thioalkenyl, C<sub>1</sub>-C<sub>9</sub> alkylamino, C<sub>2</sub>-C<sub>9</sub> alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

10 wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group.

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12. The compound of claim 11, wherein the compound is non-immunosuppressive.

25 13. The compound of claim 11, which is selected from the group consisting of:

3-phenylpropyl 2-[benzylsulfonyl]pyrazolidine-carboxylate;

30 4-phenylbutyl 2-[benzylsulfonyl]perhydropyridazine-carboxylate;

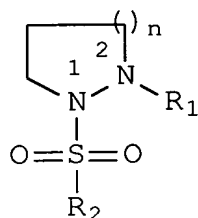
Sub  
C1  
1-(5-phenylpentanoyl)-2-(benzylsulfonyl)tetrahydro-1H-1-pyrazole; and

pharmaceutically acceptable salts, esters and solvates thereof.

5

14. A pharmaceutical composition comprising:

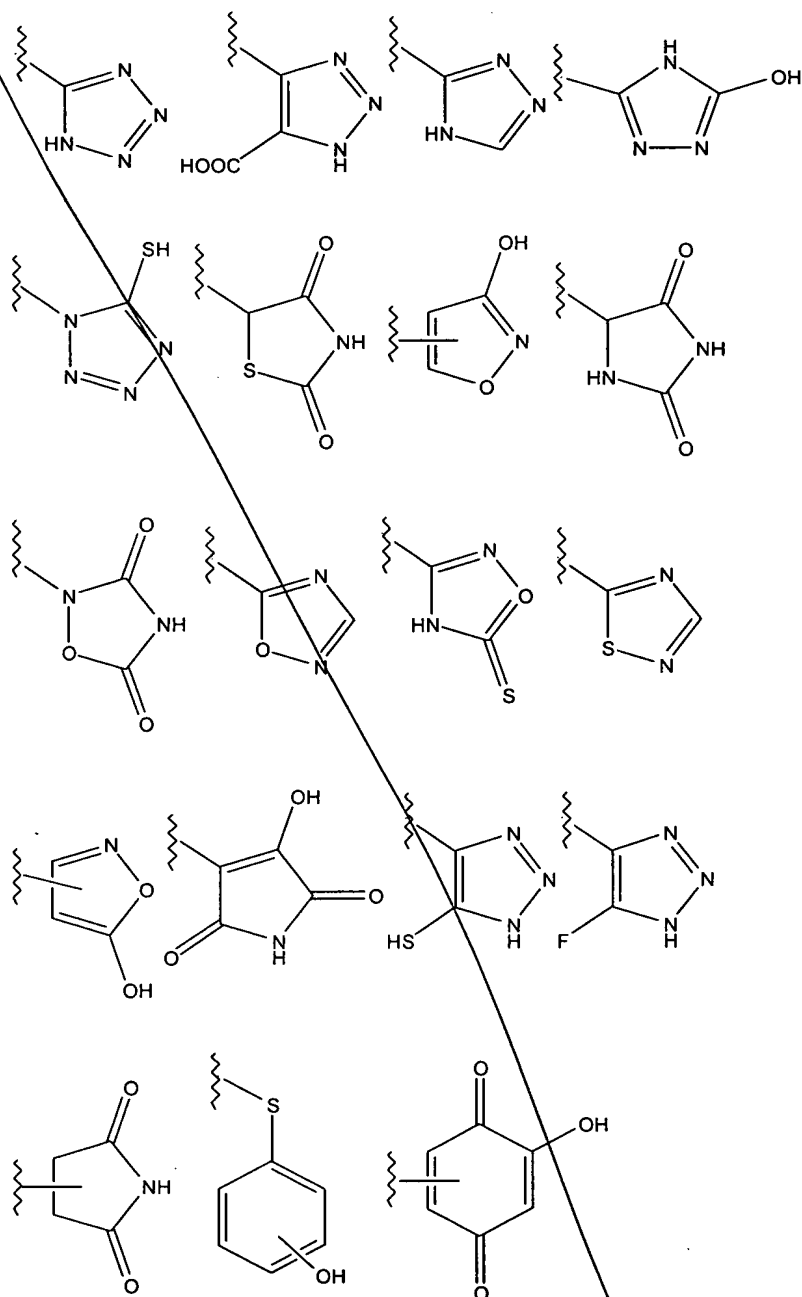
Sub  
AS  
(i) a therapeutically effective amount of a compound of formula II:



10 or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n is 1-3;

15 R<sub>1</sub> is selected from the group consisting of -CR<sub>3</sub>, -COOR<sub>3</sub>, -COR<sub>3</sub>, -COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sub>3</sub>, -PO<sub>2</sub>(R<sub>3</sub>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sub>3</sub>)<sub>2</sub>, -OR<sub>3</sub>, -SR<sub>3</sub>, -NHCOR<sub>3</sub>, -N(R<sub>3</sub>)<sub>2</sub>, -CON(R<sub>3</sub>)<sub>2</sub>, -CONH(O)R<sub>3</sub>, -CONHNHSO<sub>2</sub>R<sub>3</sub>, -COHNSO<sub>2</sub>R<sub>3</sub>, -CONR<sub>3</sub>CN,

Sub  
AS

wherein said  $R_1$  group is either unsubstituted or additionally substituted with  $R_3$ ;

5  $R_2$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  straight or branched chain alkyl,  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_2$ - $C_9$  straight or branched chain alkynyl, aryl,

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AS  
heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituents selected from R<sub>3</sub>; and

5 R<sub>3</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkynyl, C<sub>1</sub>-C<sub>9</sub> alkoxy, C<sub>2</sub>-C<sub>9</sub> alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C<sub>1</sub>-C<sub>9</sub> thioalkyl, C<sub>2</sub>-C<sub>9</sub> thioalkenyl, C<sub>1</sub>-C<sub>9</sub> alkylamino, C<sub>2</sub>-C<sub>9</sub> alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, 10 sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, 15 alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or 20 heterocycle group; and

(ii) a pharmaceutically acceptable carrier.

15. The pharmaceutical composition of claim 14, further comprising an additional neurotrophic factor.

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C1  
25 16. The pharmaceutical composition of claim 15, wherein the additional neurotrophic factor is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, 30 insulin growth factor, acidic fibroblast growth factor, basic



123

last growth factor, platelet-derived  
ropin-3, neurotrophin-4 and neurotro-

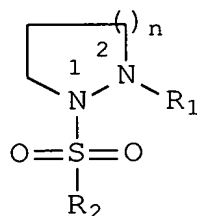
7. A method for effecting a neu-  
, comprising administering to the  
of a compound of formula II:

The diagram shows a five-membered ring with two nitrogen atoms at positions 1 and 2. The nitrogen at position 2 is substituted with an R<sub>1</sub> group. The carbon at position 3 is double-bonded to an oxygen atom and single-bonded to an R<sub>2</sub> group. The ring is labeled with numbers 1 and 2 near the nitrogens.

pharmaceutically acceptable salt,  
f, wherein:  
is 1-3;  
is selected from the group consist-  
-COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sub>3</sub>, -PO<sub>2</sub>(R<sub>3</sub>)<sub>2</sub>, -C  
NHCOR<sub>3</sub>, -N(R<sub>3</sub>)<sub>2</sub>, -CON(R<sub>3</sub>)<sub>2</sub>, -CONH(O  
R<sub>3</sub>, -CONR<sub>3</sub>CN,

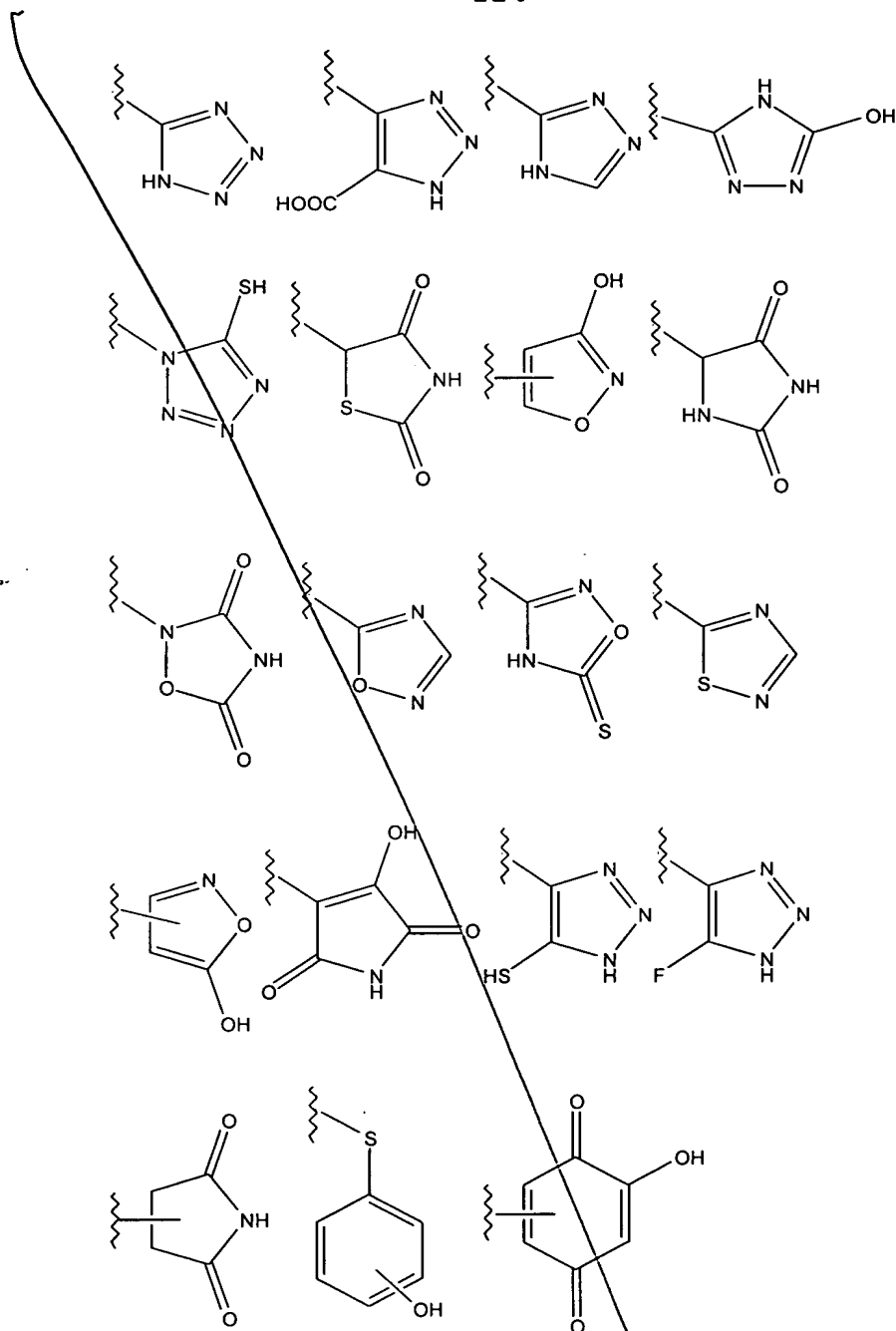
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~~R<sub>1</sub> is selected from the group consisting of -CR<sub>3</sub>, -COOR<sub>3</sub>, -COR<sub>3</sub>, -COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sub>3</sub>, -PO<sub>2</sub>(R<sub>3</sub>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sub>3</sub>)<sub>2</sub>, -OR<sub>3</sub>, -SR<sub>3</sub>, -NHCOR<sub>3</sub>, -N(R<sub>3</sub>)<sub>2</sub>, -CON(R<sub>3</sub>)<sub>2</sub>, -CONH(O)R<sub>3</sub>, -CONHNHSO<sub>2</sub>R<sub>3</sub>, -COHNSO<sub>2</sub>R<sub>3</sub>, -CONR<sub>3</sub>CN,~~



wherein said  $R_1$  group is either unsubstituted or additionally substituted with  $R_3$ ;

$R_2$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  straight or branched chain alkyl,  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_2$ - $C_9$  straight or branched chain alkynyl, aryl,

heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituents selected from R<sub>3</sub>; and

5 R<sub>3</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkynyl, C<sub>1</sub>-C<sub>9</sub> alkoxy, C<sub>2</sub>-C<sub>9</sub> alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C<sub>1</sub>-C<sub>9</sub> thioalkyl, C<sub>2</sub>-C<sub>9</sub> thioalkenyl, C<sub>1</sub>-C<sub>9</sub> alkylamino, C<sub>2</sub>-C<sub>9</sub> alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group.

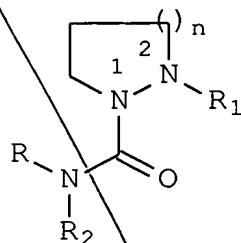
18. The method of claim 17, wherein the neuronal activity is selected from the group consisting of stimulation of damaged neurons, promotion of neuronal regeneration, prevention of neurodegeneration, and treatment of a neurological disorder.

19. The method of claim 18, wherein the neurological disorder is selected from the group consisting of peripheral neuropathy caused by physical injury or disease state,

traumatic injury to the brain, physical damage to the spinal cord, stroke associated with brain damage, and a neurological disorder relating to neurodegeneration.

5            20. The method of claim 19, wherein the neurological disorder relating to neurodegeneration is selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis.

10           21. A compound of formula III:

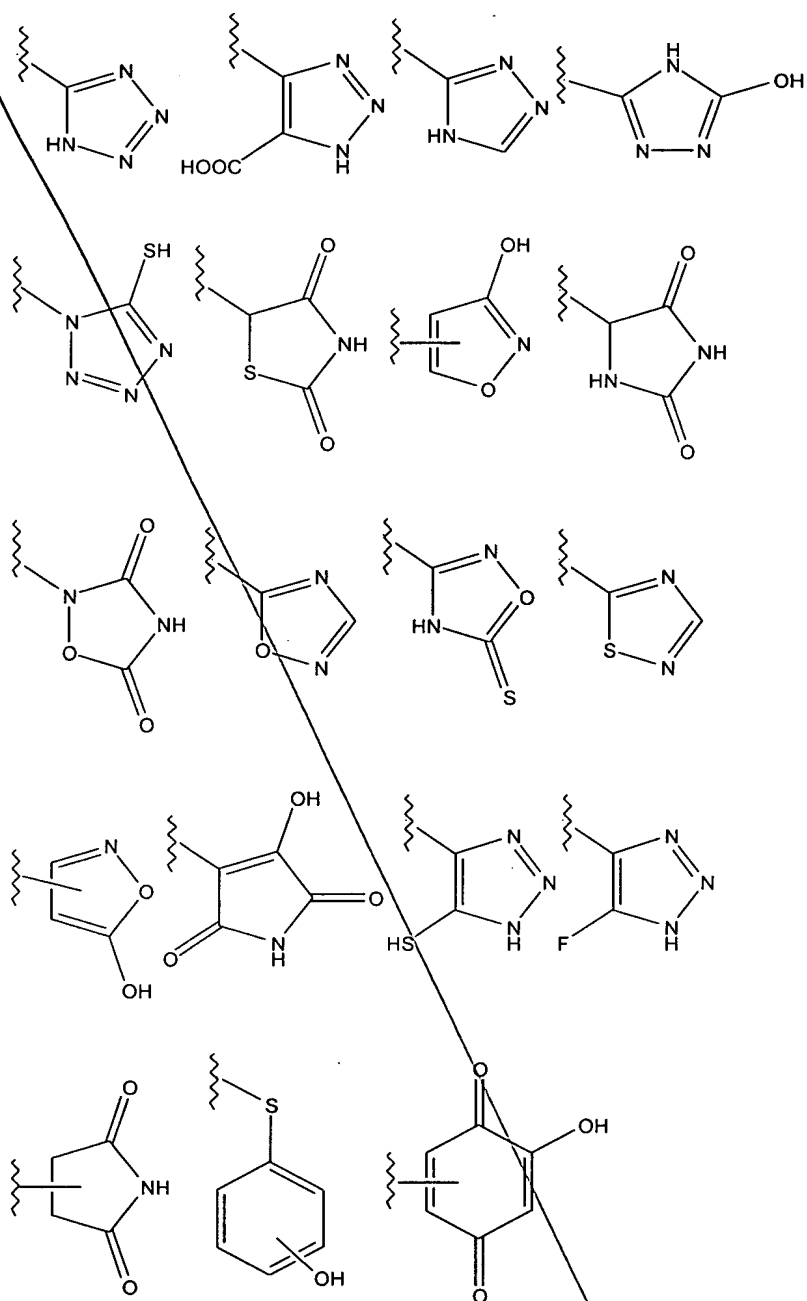


III

or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n is 1-3;

15           R<sub>1</sub> is selected from the group consisting of -CR<sub>3</sub>, -COOR<sub>3</sub>, -COR<sub>3</sub>, -COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sub>3</sub>, -PO<sub>2</sub>(R<sub>3</sub>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sub>3</sub>)<sub>2</sub>, -OR<sub>3</sub>, -SR<sub>3</sub>, -NHCOR<sub>3</sub>, -N(R<sub>3</sub>)<sub>2</sub>, -CON(R<sub>3</sub>)<sub>2</sub>, -CONH(O)R<sub>3</sub>, -CONHNHSO<sub>2</sub>R<sub>3</sub>, -COHNSO<sub>2</sub>R<sub>3</sub>, -CONR<sub>3</sub>CN,



wherein said  $R_1$  group is either unsubstituted or additionally substituted with  $R_3$ ;

$R$  and  $R_2$  are independently  $C_1$ - $C_9$  alkyl,  $C_2$ - $C_9$  alkenyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, aryl, heteroaryl, carbocycle, or heterocycle

is unsubstituted or substituted with one or more substituent(s) selected from R<sub>3</sub>; and

R<sub>3</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkynyl, C<sub>1</sub>-C<sub>9</sub> alkoxy, C<sub>2</sub>-C<sub>9</sub> alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C<sub>1</sub>-C<sub>9</sub> thioalkyl, C<sub>2</sub>-C<sub>9</sub> thioalkenyl, C<sub>1</sub>-C<sub>9</sub> alkylamino, C<sub>2</sub>-C<sub>9</sub> alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group.

22. The compound of claim 21, wherein the compound is non-immunosuppressive.

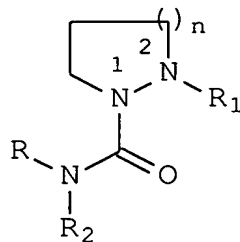
23. The compound of claim 21, wherein said compound is 1-(5-phenylpentanoyl)-2-(N,N-dicyclohexylcarbamoyl)-tetrahydro-1H-1-pyrazole or a pharmaceutically acceptable salt, ester or solvate thereof.

24. A pharmaceutical composition comprising:

(i) a therapeutically effective amount of a compound of

formula III:

III

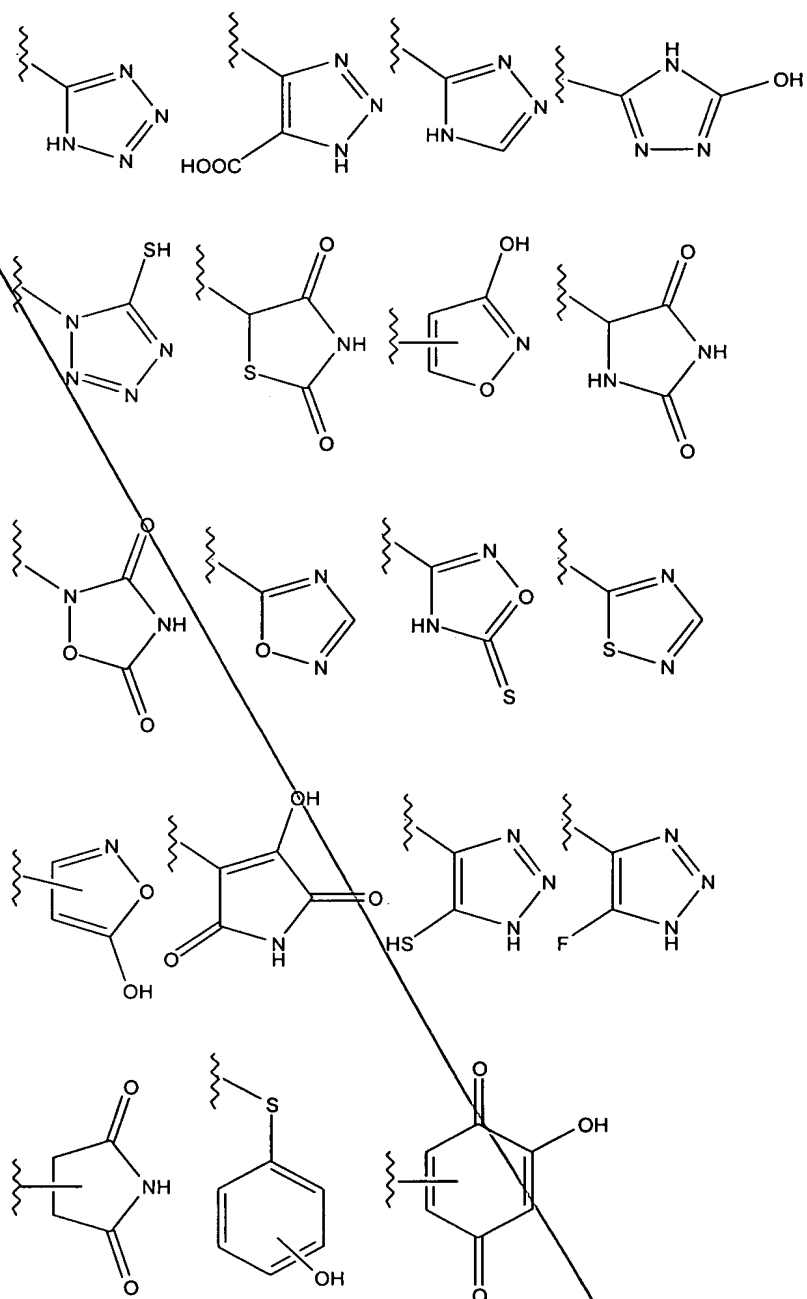


or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

5            n is 1-3;

R<sub>1</sub> is selected from the group consisting of -CR<sub>3</sub>, -COOR<sub>3</sub>, -COR<sub>3</sub>, -COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sub>3</sub>, -PO<sub>2</sub>(R<sub>3</sub>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sub>3</sub>)<sub>2</sub>, -OR<sub>3</sub>, -SR<sub>3</sub>, -NHCOR<sub>3</sub>, -N(R<sub>3</sub>)<sub>2</sub>, -CON(R<sub>3</sub>)<sub>2</sub>, -CONH(O)R<sub>3</sub>, -CONHNHSO<sub>2</sub>R<sub>3</sub>, -COHNSO<sub>2</sub>R<sub>3</sub>, -CONR<sub>3</sub>CN,

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R and R<sub>2</sub> are independently C<sub>1</sub>-C<sub>9</sub> alkyl, C<sub>2</sub>-C<sub>9</sub> alkenyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, aryl, heteroaryl, carbocycle, or heterocycle



is unsubstituted or substituted with one or more substituent(s) selected from R<sub>3</sub>; and

R<sub>3</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkynyl, C<sub>1</sub>-C<sub>9</sub> alkoxy, C<sub>2</sub>-C<sub>9</sub> alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C<sub>1</sub>-C<sub>9</sub> thioalkyl, C<sub>2</sub>-C<sub>9</sub> thioalkenyl, C<sub>1</sub>-C<sub>9</sub> alkylamino, C<sub>2</sub>-C<sub>9</sub> alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

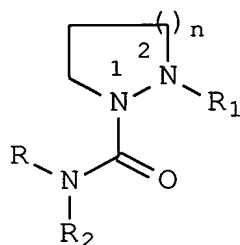
wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group; and

(ii) a pharmaceutically acceptable carrier.

25. The pharmaceutical composition of claim 24, further comprising an additional neurotrophic factor.

26. The pharmaceutical composition of claim 25, wherein the additional neurotrophic factor is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factor, neurotrophin-3, neurotrophin-4 and neurotrophin-5.

27. A method for effecting a neuronal activity in a mammal, comprising administering to the mammal an effective amount of a compound of formula III:



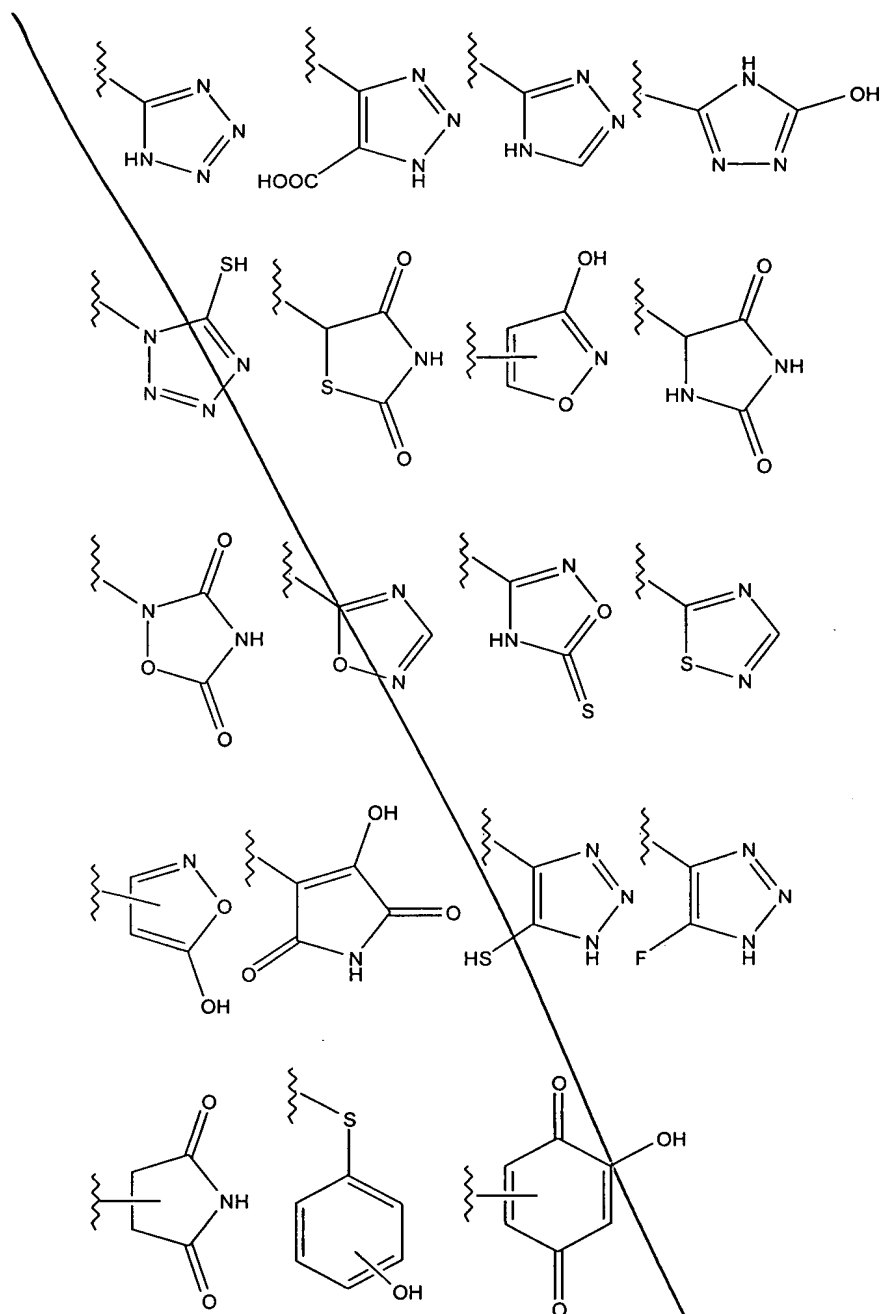
III

5 or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n is 1-3;

10 R<sub>1</sub> is selected from the group consisting of -CR<sub>3</sub>, -COOR<sub>3</sub>, -COR<sub>3</sub>, -COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sub>3</sub>, -PO<sub>2</sub>(R<sub>3</sub>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sub>3</sub>)<sub>2</sub>, -OR<sub>3</sub>, -SR<sub>3</sub>, -NHCOR<sub>3</sub>, -N(R<sub>3</sub>)<sub>2</sub>, -CON(R<sub>3</sub>)<sub>2</sub>, -CONH(O)R<sub>3</sub>, -CONHNHSO<sub>2</sub>R<sub>3</sub>, -COHNSO<sub>2</sub>R<sub>3</sub>, -CONR<sub>3</sub>CN,

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wherein said R<sub>1</sub> group is either unsubstituted or substituted with one or more substituent(s);

5 R and R<sub>2</sub> are independently C<sub>1</sub>-C<sub>9</sub> alkyl, C<sub>2</sub>-C<sub>9</sub> alkenyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, aryl, heteroaryl, carbocycle, or heterocycle

is unsubstituted or substituted with one or more substituent(s); and

*Sub a*  
 R<sub>3</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkynyl, C<sub>1</sub>-C<sub>9</sub> alkoxy, C<sub>2</sub>-C<sub>9</sub> alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C<sub>1</sub>-C<sub>9</sub> thioalkyl, C<sub>2</sub>-C<sub>9</sub> thioalkenyl, C<sub>1</sub>-C<sub>9</sub> alkylamino, C<sub>2</sub>-C<sub>9</sub> alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group.

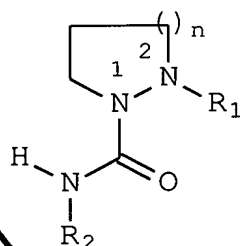
28. The method of claim 27, wherein the neuronal activity is selected from the group consisting of stimulation of damaged neurons, promotion of neuronal regeneration, prevention of neurodegeneration, and treatment of a neurological disorder.

29. The method of claim 28, wherein the neurological disorder is selected from the group consisting of peripheral neuropathy caused by physical injury or disease state, traumatic injury to the brain, physical damage to the spinal cord, stroke associated with brain damage, and a neurological

disorder relating to neurodegeneration.

30. The method of claim 29, wherein the neurological disorder relating to neurodegeneration is selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis.

31. A compound of formula IV:

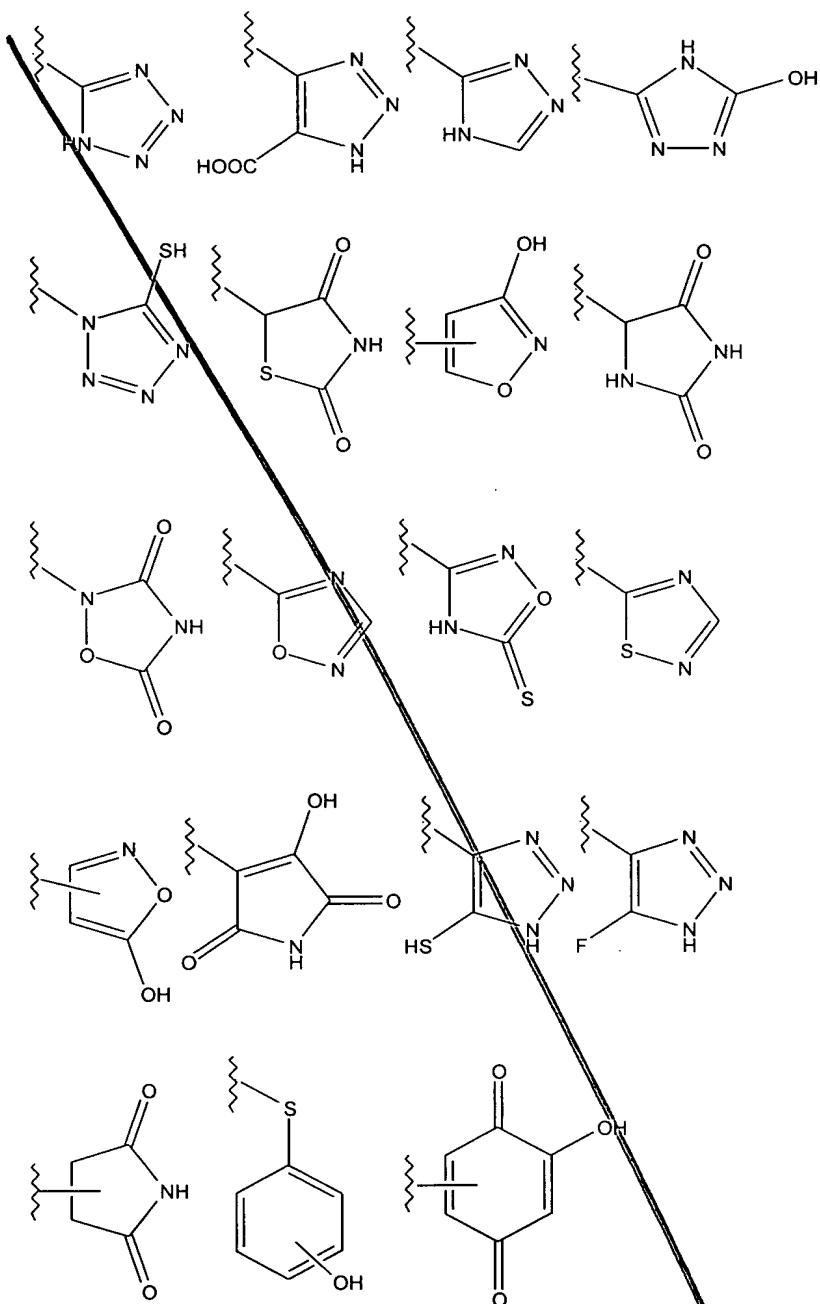


IV

or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

$n$  is 1-3;

$R_1$  is selected from the group consisting of  $-CR_3$ ,  $-COOR_3$ ,  $-COR_3$ ,  $-COOH$ ,  $-SO_3H$ ,  $-SO_2HNR_3$ ,  $-PO_2(R_3)_2$ ,  $-CN$ ,  $-PO_3(R_3)_2$ ,  $-OR_3$ ,  $-SR_3$ ,  $-NHCOR_3$ ,  $-N(R_3)_2$ ,  $-CON(R_3)_2$ ,  $-CONH(O)R_3$ ,  $-CONHNHSO_2R_3$ ,  $-COHNSO_2R_3$ ,  $-CONR_3CN$ ,



wherein said  $R_1$  group is either unsubstituted or additionally substituted with  $R_3$ ; and

5  $R_2$  is  $C_1$ - $C_9$  alkyl,  $C_2$ - $C_9$  alkenyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, aryl, heteroaryl, carbocycle, or heterocycle is substituted with one

or more substituent(s) selected from R<sub>3</sub>; and

R<sub>3</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkynyl, C<sub>1</sub>-C<sub>9</sub> alkoxy, C<sub>2</sub>-C<sub>9</sub> alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C<sub>1</sub>-C<sub>9</sub> thioalkyl, C<sub>2</sub>-C<sub>9</sub> thioalkenyl, C<sub>1</sub>-C<sub>9</sub> alkylamino, C<sub>2</sub>-C<sub>9</sub> alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group.

32. The compound of claim 31, wherein the compound is non-immunosuppressive.

33. The compound of claim 31, wherein said compound is selected from the group consisting of:

3-phenylpropyl 2-(N-cyclohexylcarbamoyl)pyrazolidine-carboxylate;

4-phenylbutyl 2-(N-cyclohexylcarbamoyl)perhydro-pyridazinecarboxylate;

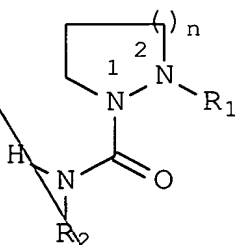
1-(5-phenylpentanoyl)-2-(N-cyclohexylcarbamoyl)-tetrahydro-1H-1-pyrazole; and

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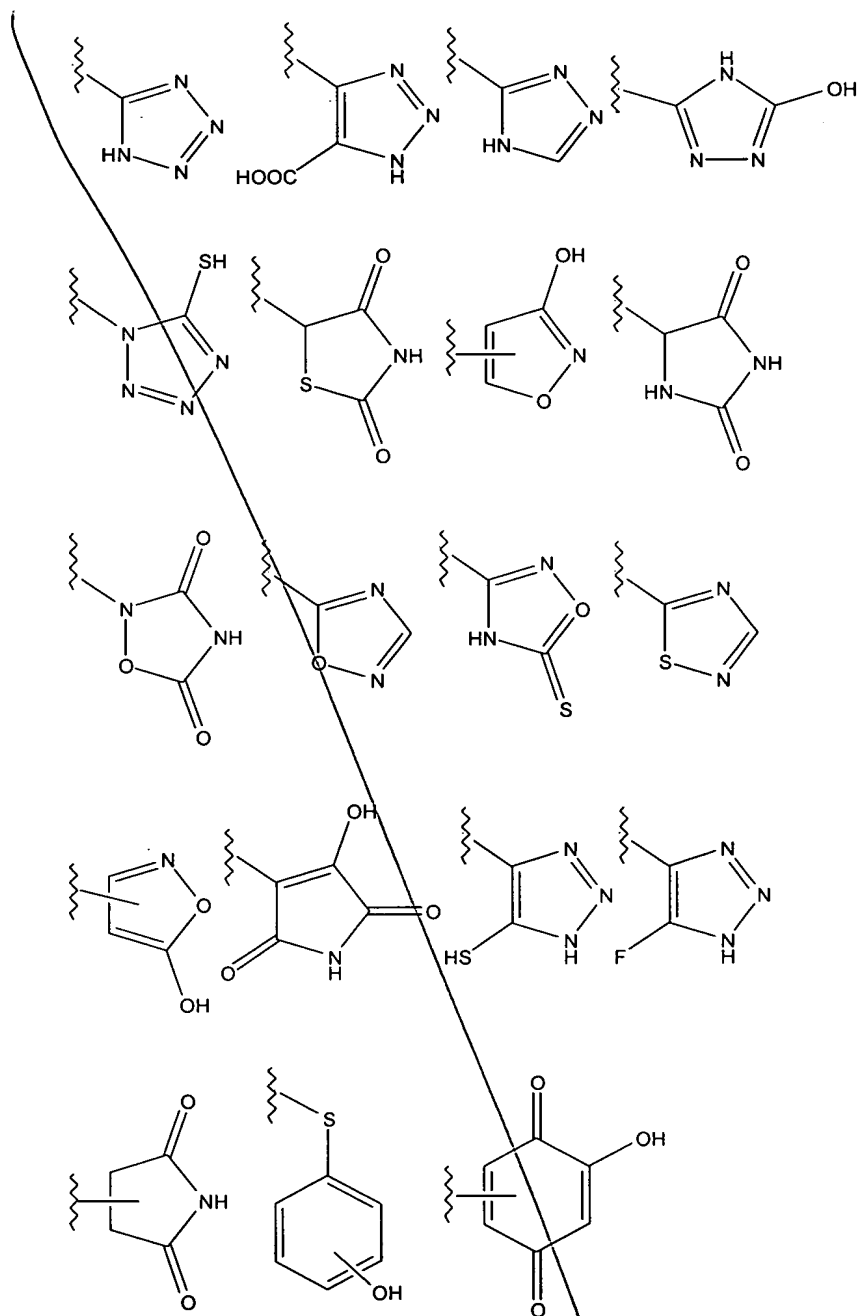
or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

~~R<sub>1</sub> is selected from the group consisting of -CR<sub>3</sub>, -COOR<sub>3</sub>, -COR<sub>3</sub>, -COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sub>3</sub>, -PO<sub>2</sub>(R<sub>3</sub>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sub>3</sub>)<sub>2</sub>, -OR<sub>3</sub>, -SR<sub>3</sub>, -NHCOR<sub>3</sub>, -N(R<sub>3</sub>)<sub>2</sub>, -CON(R<sub>3</sub>)<sub>2</sub>, -CONH(O)R<sub>3</sub>, -CONHNHSO<sub>2</sub>R<sub>3</sub>, -COHNSO<sub>2</sub>R<sub>3</sub>, -CONR<sub>3</sub>CN,~~



IV





wherein said R<sub>1</sub> group is either unsubstituted or additionally substituted with R<sub>3</sub>; and

5           R<sub>2</sub> is C<sub>1</sub>-C<sub>9</sub> alkyl, C<sub>2</sub>-C<sub>9</sub> alkenyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, aryl, heteroaryl, carbocycle, or heterocycle is substituted with one

or more substituent(s) selected from R<sub>3</sub>; and

R<sub>3</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkynyl, C<sub>1</sub>-C<sub>9</sub> alkoxy, C<sub>2</sub>-C<sub>9</sub> alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C<sub>1</sub>-C<sub>9</sub> thioalkyl, C<sub>2</sub>-C<sub>9</sub> thioalkenyl, C<sub>1</sub>-C<sub>9</sub> alkylamino, C<sub>2</sub>-C<sub>9</sub> alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

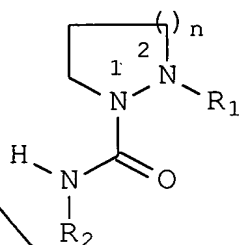
wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group; and

(ii) a pharmaceutically acceptable carrier.

35. The pharmaceutical composition of claim 34, further comprising an additional neurotrophic factor.

36. The pharmaceutical composition of claim 35, wherein the additional neurotrophic factor is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factor, neurotrophin-3, neurotrophin-4 and neurotrophin-5.

Sub



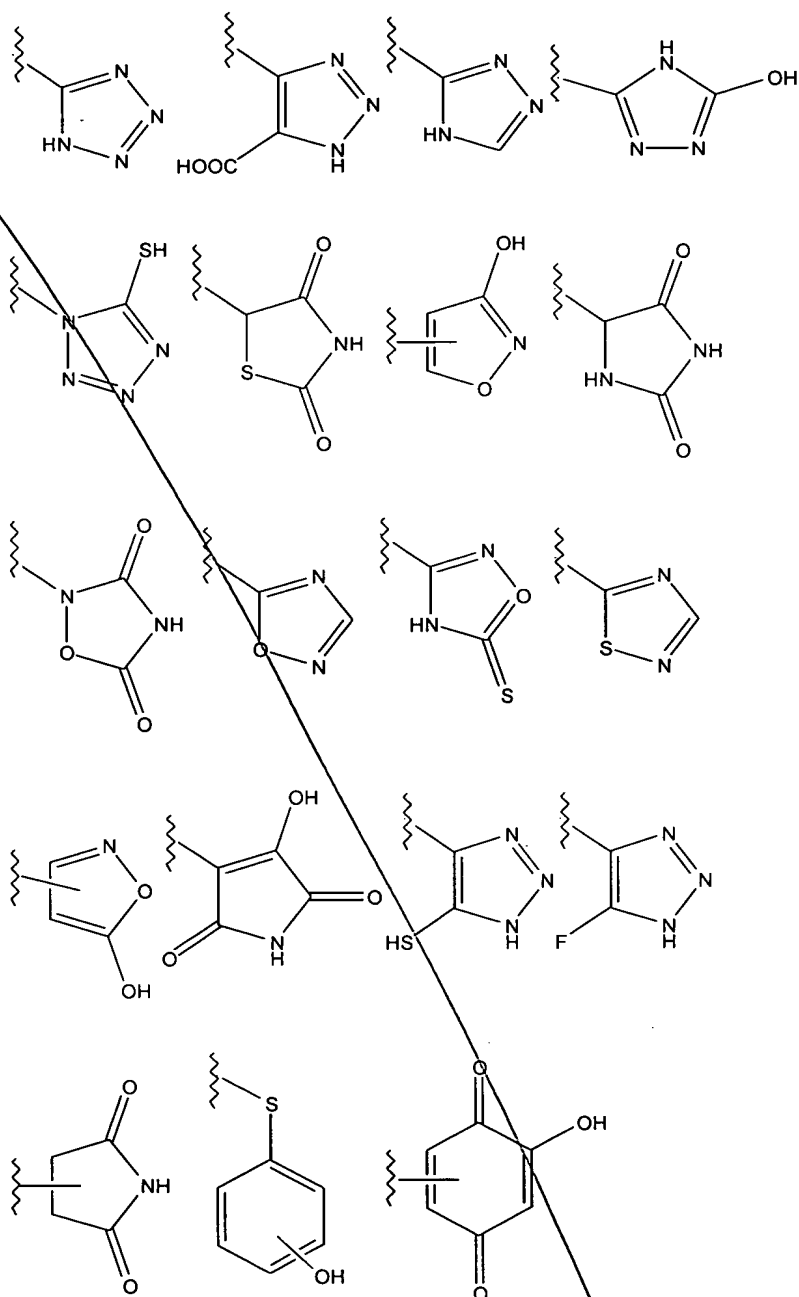
IV

or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n is 1-3;

~~R<sub>1</sub> is selected from the group consisting of -CR<sub>3</sub>, -COOR<sub>3</sub>, -COR<sub>3</sub>, -COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sub>3</sub>, -PO<sub>2</sub>(R<sub>3</sub>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sub>3</sub>)<sub>2</sub>, -OR<sub>3</sub>, -SR<sub>3</sub>, -NHCOR<sub>3</sub>, -N(R<sub>3</sub>)<sub>2</sub>, -CON(R<sub>3</sub>)<sub>2</sub>, -CONH(O)R<sub>3</sub>, -CONHNHSO<sub>2</sub>R<sub>3</sub>, -COHNSO<sub>2</sub>R<sub>3</sub>, -CONR<sub>3</sub>CN,~~

[illegible]



wherein said  $R_1$  group is either unsubstituted or additionally substituted with  $R_3$ ; and

$R_2$  is  $C_1$ - $C_9$  alkyl,  $C_2$ - $C_9$  alkenyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, aryl, heteroaryl, carbocycle, or heterocycle is substituted with one

or more substituent(s) selected from R<sub>3</sub>; and

R<sub>3</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkynyl, C<sub>1</sub>-C<sub>9</sub> alkoxy, C<sub>2</sub>-C<sub>9</sub> alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C<sub>1</sub>-C<sub>9</sub> thioalkyl, C<sub>2</sub>-C<sub>9</sub> thioalkenyl, C<sub>1</sub>-C<sub>9</sub> alkylamino, C<sub>2</sub>-C<sub>9</sub> alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group.

38. The method of claim 37, wherein the neuronal activity is selected from the group consisting of stimulation of damaged neurons, promotion of neuronal regeneration, prevention of neurodegeneration and treatment of a neurological disorder.

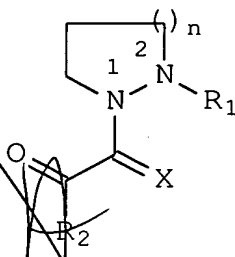
39. The method of claim 38, wherein the neurological disorder is selected from the group consisting of peripheral neuropathy caused by physical injury or disease state, traumatic injury to the brain, physical damage to the spinal cord, stroke associated with brain damage, and a neurological disorder relating to neurodegeneration.

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40. The method of claim 39, wherein the neurological disorder relating to neurodegeneration is selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease and amyotrophic lateral sclerosis.

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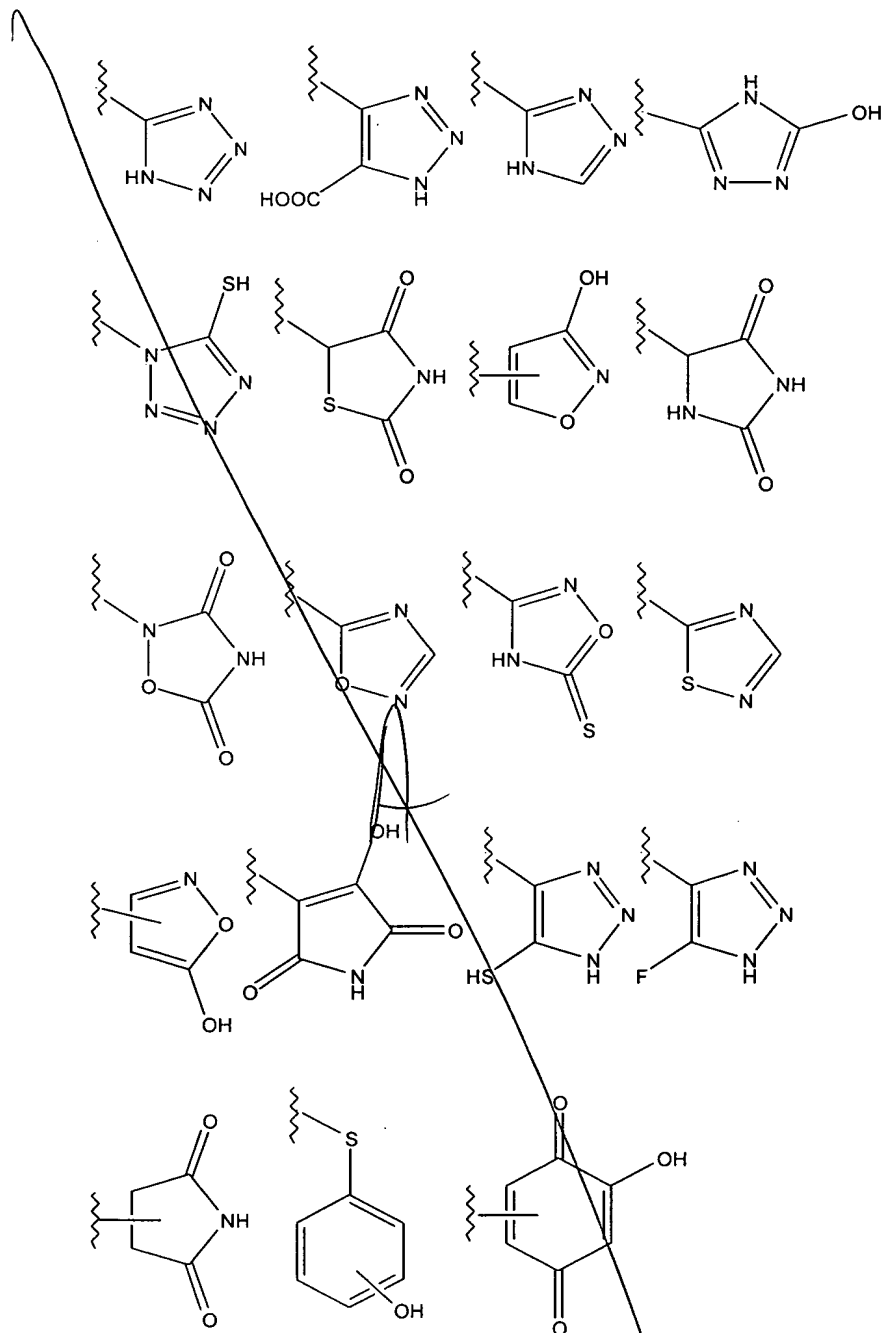
41. A process for preparing a compound having the formula (I):



10 or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n is 1-3;

15 R<sub>1</sub> is selected from the group consisting of -CR<sub>3</sub>, -COOR<sub>3</sub>, -COR<sub>3</sub>, -COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sub>3</sub>, -PO<sub>2</sub>(R<sub>3</sub>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sub>3</sub>)<sub>2</sub>, -OR<sub>3</sub>, -SR<sub>3</sub>, -NHCOR<sub>3</sub>, -N(R<sub>3</sub>)<sub>2</sub>, -CON(R<sub>3</sub>)<sub>2</sub>, -CONH(O)R<sub>3</sub>, -CONHNHSO<sub>2</sub>R<sub>3</sub>, -COHNSO<sub>2</sub>R<sub>3</sub>, -CONR<sub>3</sub>CN,



wherein said R<sub>1</sub> group is either unsubstituted or additionally substituted with R<sub>3</sub>;

5 R<sub>2</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkynyl, aryl,

heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituents selected from  $R_3$ ;

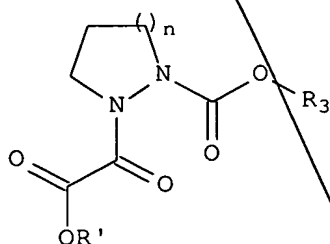
$R_3$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  alkyl,  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_2$ - $C_9$  straight or branched chain alkynyl,  $C_1$ - $C_9$  alkoxy,  $C_2$ - $C_9$  alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy,  $C_1$ - $C_9$  thioalkyl,  $C_2$ - $C_9$  thioalkenyl,  $C_1$ - $C_9$  alkylamino,  $C_2$ - $C_9$  alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group; and

X is O,

which process comprises (1):

(a) reacting a compound of the formula:



with a compound of the formula  $R_2$ -Mg-X, wherein

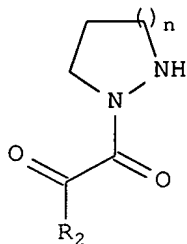


R' is a straight or branched chain alkyl group which is optionally substituted in one or more positions;

X is halogen; and

n, R<sub>3</sub>, and R<sub>2</sub> are as defined above; or

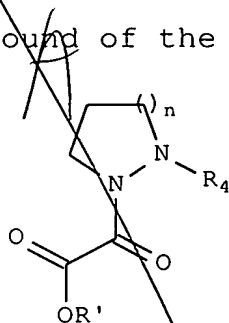
5 (b) reacting a compound of the formula:



with a compound of the formula R<sub>3</sub>COOH or activated derivatives thereof, wherein

n, R<sub>3</sub>, and R<sub>2</sub> are as defined above; or

10 (c) reacting a compound of the formula:



with a compound of the formula R<sub>2</sub>-Mg-X, wherein

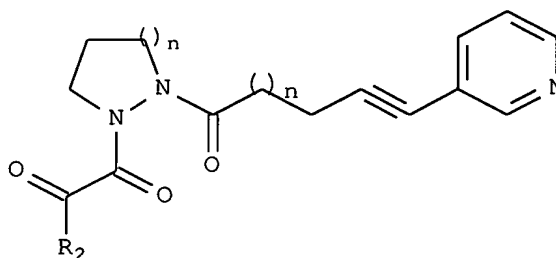
R' is a straight or branched chain alkyl group which is optionally substituted in one or more positions;

15 R<sub>4</sub> is an alkyl group substituted with an aryl group;

X is halogen; and

n and R<sub>2</sub> are as defined above; or

(d) reducing a compound of the formula:



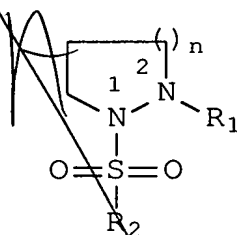
wherein

$n$  and  $R_2$  are as defined above,

and, if desired,

5 (2) removing a protecting group from the product.

42. A process for preparing a compound having the formula (II):

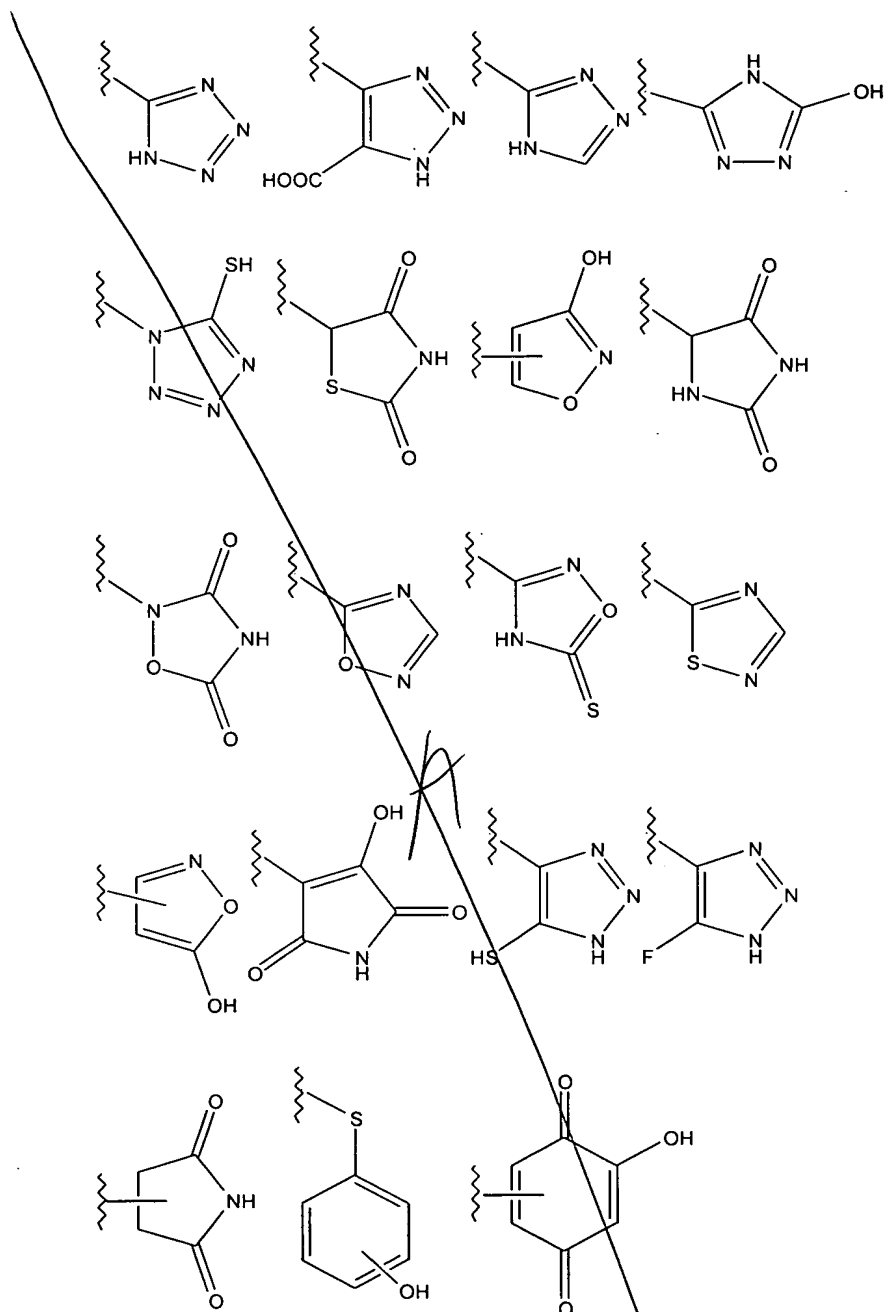


II

10 or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

$n$  is 1-3;

15  $R_1$  is selected from the group consisting of  $-CR_3$ ,  $-COOR_3$ ,  $-COR_3$ ,  $-COOH$ ,  $-SO_3H$ ,  $-SO_2HNR_3$ ,  $-PO_2(R_3)_2$ ,  $-CN$ ,  $-PO_3(R_3)_2$ ,  $-OR_3$ ,  $-SR_3$ ,  $-NHCOR_3$ ,  $-N(R_3)_2$ ,  $-CON(R_3)_2$ ,  $-CONH(O)R_3$ ,  $-CONHNHSO_2R_3$ ,  $-COHNSO_2R_3$ ,  $-CONR_3CN$ ,



wherein said R<sub>1</sub> group is either unsubstituted or additionally substituted with R<sub>3</sub>;

R<sub>2</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkynyl, aryl,

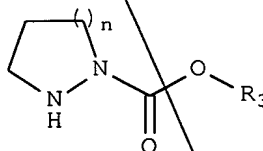
heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituents selected from  $R_3$ ; and

$R_3$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  alkyl,  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_2$ - $C_9$  straight or branched chain alkynyl,  $C_1$ - $C_9$  alkoxy,  $C_2$ - $C_9$  alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy,  $C_1$ - $C_9$  thioalkyl,  $C_2$ - $C_9$  thioalkenyl,  $C_1$ - $C_9$  alkylamino,  $C_2$ - $C_9$  alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

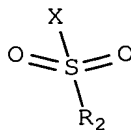
wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group,

which process comprises (1):

reacting a compound of the formula:



with a compound of the formula:



wherein

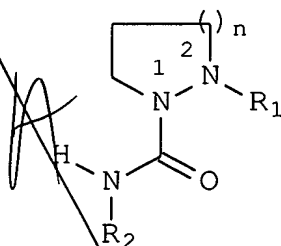
X is halogen; and

n, R<sub>3</sub>, and R<sub>2</sub> are as defined above,

and, if desired,

(2) removing a protecting group from the product.

43. A process for preparing a compound having the formula (IV):

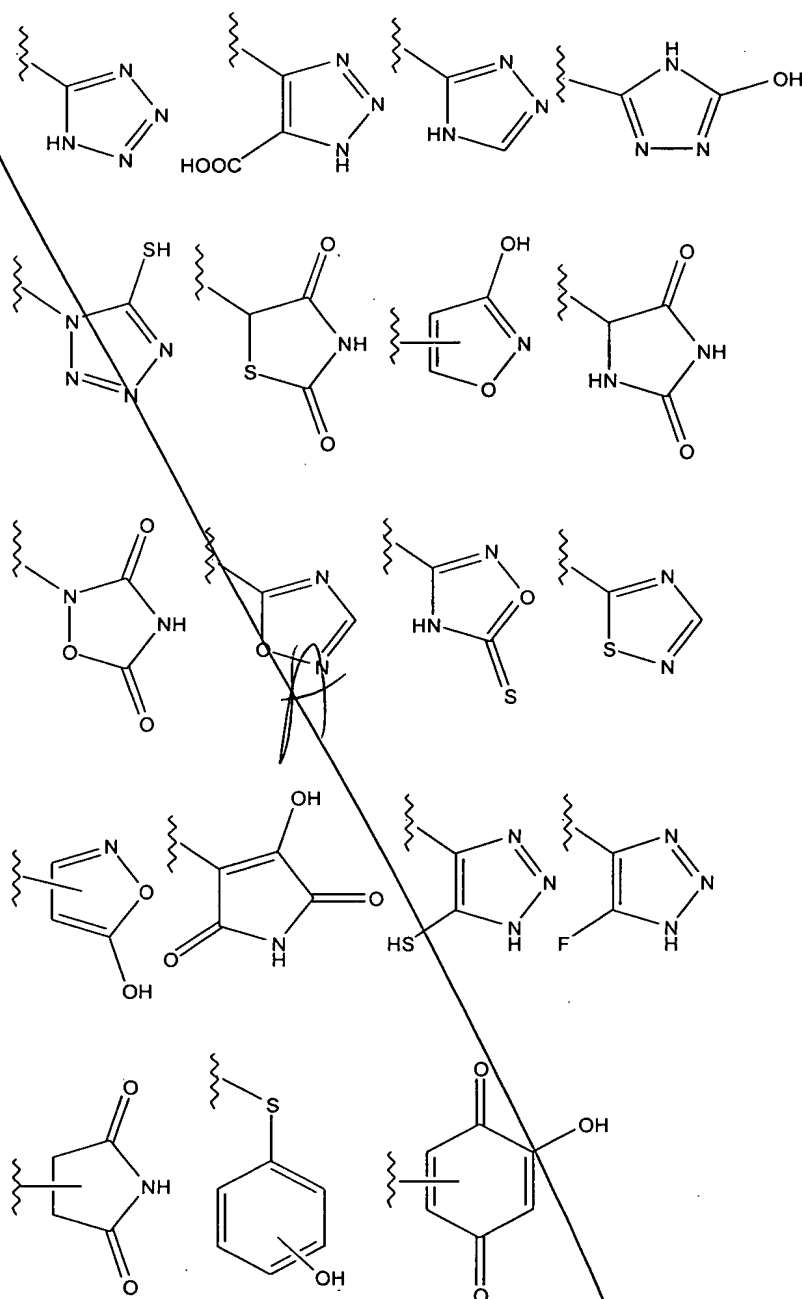


IV

or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n is 1-3;

R<sub>1</sub> is selected from the group consisting of -CR<sub>3</sub>, -COOR<sub>3</sub>, -COR<sub>3</sub>, -COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sub>3</sub>, -PO<sub>2</sub>(R<sub>3</sub>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sub>3</sub>)<sub>2</sub>, -OR<sub>3</sub>, -SR<sub>3</sub>, -NHCOR<sub>3</sub>, -N(R<sub>3</sub>)<sub>2</sub>, -CON(R<sub>3</sub>)<sub>2</sub>, -CONH(O)R<sub>3</sub>, -CONHNHSO<sub>2</sub>R<sub>3</sub>, -COHNSO<sub>2</sub>R<sub>3</sub>, -CONR<sub>3</sub>CN,



wherein said  $R_1$  group is either unsubstituted or additionally substituted with  $R_3$ ; and

5  $R_2$  is  $C_1$ - $C_9$  alkyl,  $C_2$ - $C_9$  alkenyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, aryl, heteroaryl, carbocycle, or heterocycle is substituted with one

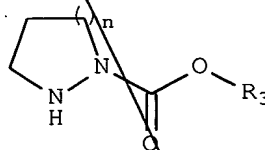
or more substituent(s) selected from  $R_3$ ; and

$R_3$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  alkyl,  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_2$ - $C_9$  straight or branched chain alkynyl,  $C_1$ - $C_9$  alkoxy,  $C_2$ - $C_9$  alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy,  $C_1$ - $C_9$  thioalkyl,  $C_2$ - $C_9$  thioalkenyl,  $C_1$ - $C_9$  alkylamino,  $C_2$ - $C_9$  alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

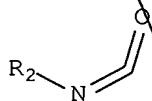
wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group,

which process comprises (1):

reacting a compound of the formula:



with a compound of the formula:



wherein

$n$ ,  $R_3$ , and  $R_2$  are as defined above,

and, if desired,

(2) removing a protecting group from the product.

add

At

TOCTO 000000